Examiner: Leigh C. Maier Group Art Unit: 1623

This listing of claims replaces all prior versions and listings of claims in the application. The amendments to pending claims 1, 50, and 52-55 that are requested herein are illustrated in this listing, and pending claim 61 is shown as cancelled, as discussed further below.

## **Listing of Claims**

# 1. (Currently Amended) A compound of the Formula I

$$\begin{array}{c|c} R^1 & O & O \\ \hline & N & O & R^2 \\ \hline & O & & I \end{array}$$

wherein R1 is

$$R^{3}O - C - ,$$
 $R^{3} - C - ,$ 
 $R^{3} - C - ,$ 

$$R^{aO}$$
,  $O$ 
 $NH_{2}$ 

Examiner: Leigh C. Maier Group Art Unit: 1623

each Ra is independently hydrogen, C1-C6 alkyl, or -(CH2)n aryl;

$$R^2$$
 is — $(CRR)_n$ -aryl,

$$-(CRR)_n$$
-(substituted-aryl),

$$-(CRR)_n$$
-aryl- $(CH_2)_n$ -aryl,

$$-(CRR)_n$$
-CH(aryl)<sub>2</sub>.

$$-(CRR)_n$$
  $-CH$   $(CH_2)_n$   $-aryl$   $(CH_2)_n$   $-aryl$ 

$$-(CRR)_n$$
— $CH$ 
 $(CH_2)_n$ —substituted aryle
 $(CH_2)_n$ —aryle

$$-(CRR)_n$$

Application No. 09/284,424, filed 9 April 1999 Amendment and Response of 23 October 2003 Responsive to Office Action of 23 April 2003

each R is independently hydrogen,  $C_1\text{-}C_6$  alkyl, halogen or hydroxy;

X is O or S;

Examiner: Leigh C. Maier Group Art Unit: 1623

$$R^3$$
 is  $C_1$ - $C_6$  alkyl,

aryl,

—(CHR)<sub>n</sub>-aryl,

—(CHR)<sub>n</sub>-substituted aryl,

$$-(CRR)_n$$
 $-C$  $-OR$  $^a$ ,

$$--(CRR)_nO(CH_2)_n$$
-aryl,

cycloalkyl,

substituted cycloalkyl,

$$-(CRR)_n - \overset{O}{C} - NR^aR^a,$$

$$-(CRR)_n - \begin{matrix} O \\ II \\ -S \\ II \\ O \end{matrix} (CH_2)_n \text{ aryl}$$

$$-(CRR)_n - \begin{matrix} O \\ II \\ S - C_1 - C_6 \text{ alkyl} \\ O \end{matrix}$$

$$-(CRR)_nS(CH_2)_nCOR^a$$

$$\begin{array}{c} O & O \\ \parallel & \parallel \\ -(CRR)_nS(CH_2)_nCOR^a \\ \parallel & 0 \\ -(CRR)_nS(CH_2)_n-aryl \\ O & , \\ -(CRR)_nS(CH_2)_n-aryl \\ O & , \\ -(CRR)_nS(CH_2)_n-aryl \\ O & , \\ -(CRR)_nS(CH_2)_n aryl \\ -(CRR)_nS(CH_2)_n CO_2R^a, \\ -(CRR)_nS(CH_2)_nCO_2R^a, \\ -(CH_2)_nNHCC_1-C_6 alkyl \\ -(CH_2)_nCNR^bR^b, \\ O & & \\ -(CH_2)_nCNR^bR^b, \\ \end{array}$$

each R' is independently  $C_1$ - $C_6$  alkyl,  $C_1$ - $C_6$  alkylaryl,

Examiner: Leigh C. Maier Group Art Unit: 1623

aryl, or

hydrogen;

each J is independently

- $-CO_2R^b$ ,
- —CONRbRb,
- -SO<sub>2</sub>NR<sup>b</sup>R<sup>b</sup>, or
- $-SO_2R^b$ ;

each R<sup>b</sup> is independently hydrogen, C<sub>1</sub>-C<sub>6</sub> alkyl, aryl, substituted aryl, arylalkyl, or substituted arylalkyl;

R<sup>4</sup> is hydrogen,

C<sub>1</sub>-C<sub>6</sub> alkyl,

-phenyl, or

$$C_1$$
- $C_6$  alkyl- $C$ -

 $R^5$  is  $C_1$ - $C_6$  alkyl-CO—,

$$--(CH2)naryl,$$

$$C_1$$
- $C_6$  alkyl $O$ - $C$ -

$$C_1$$
- $C_6$ -alkyl- $X$ - $(CH_2)_nCO$ ,

$$C_1$$
- $C_6$  alkyl- $X$ - $(CH_2)_nO$ - $C$ -

$$\begin{array}{c} O \\ II \\ -C(CRR)_n aryl \end{array},$$

$$-\frac{O}{CNR^aR^a}$$
,

$$\begin{array}{c} \overset{O}{\overset{\parallel}{\underset{\parallel}{-}}} \overset{\square}{\underset{\parallel}{\text{SC}}} _{1}\text{-}C_{6} \text{ alkyl} \\ \overset{\square}{\underset{O}{\text{O}}} \end{array}$$

$$\begin{array}{c} O & O \\ \parallel & \parallel \\ -C(CH_2)_nCNR^aR^a \end{array}$$

$$\begin{array}{c} O \\ II \\ --CO(CH_2)_n \text{ aryl} \end{array},$$

$${\rm CO}_{II}^{O}$$
 —  ${\rm CO}({\rm CH_2})_n$  substituted aryl,

$$\begin{array}{ccc} O & O \\ \parallel & \parallel \\ -C(CRR)_nNHCO(CH_2)_n-aryl \end{array},$$

$$-\overset{O}{\overset{\parallel}{\underset{R^6}{\subset}}}-\overset{CH-N}{\overset{R^a}{\underset{R^{5a}}{\subset}}},$$

$$--(CH_2)_nX(CH_2)_n$$
-aryl, or

$$\begin{matrix} R^{5a} \text{ is} \\ \begin{matrix} O \\ II \\ --CC_1\text{-}C_6 \text{ alkyl} \end{matrix},$$

$$-COC_1-C_6$$
 alkyl

$$O$$
 $\parallel$ 
 $CO(CH_2)_n$  aryl , or

 $R^6$  is hydrogen,  $C_1$ - $C_6$  alkyl, — $(CH_2)_n$  aryl, — $(CH_2)_nCO_2R^a$ , or hydroxyl substituted  $C_1$ - $C_6$  alkyl;

each n is independently 0 to 3, and the pharmaceutically acceptable salts thereof;

excluding the following compounds:

N-(3-Phenylpropionyl)-L-valine-L-alanine-L-aspartic acid 2,6-dihydroxy-benzoyloxy methyl ketone;

N-(3-Phenylpropionyl)-L-valine-L-alanine-L-aspartic acid 2,6-dimethyl-benzoyloxy methyl ketone;

N-Benzyloxycarbonyl-L-aspartic acid 2,6-dichlorobenzoyloxymethyl ketone;

N-Benzyloxycarbonyl-L-aspartic acid 2,6-ditrifluoromethyl benzoyloxymethyl ketone;

N-Benzyloxycarbonyl-L-aspartic acid 2,6-dimethoxybenzoyloxy methyl ketone;

N-Benzyloxycarbonyl-L-aspartic acid 2,6-dichloro-3-(benzyloxy)benzoyloxy-methyl ketone;

N-Benzyloxycarbonyl-L-aspartic acid 2-acetamido-6-chlorobenzoyloxymethyl ketone;

N-Benzyloxycarbonyl-L-aspartic acid 2,6-difluorobenzoyloxymethyl ketone;

N-Benzyloxycarbonyl-L-aspartic acid 3-(N-butylsulfonamido)-2,6-dichlorobenzoyloxy methyl ketone;

N-Benzyloxycarbonyl-L-aspartic acid 2,6-dichloro-3-sulfonamido benzoyloxy

- methyl ketone;
- N-Benzyloxycarbonyl-L-aspartic acid 3-(N-benzylsulfonamido)-2,6-dichlorobenzoyloxy methyl ketone;

- N-Benzyloxycarbonyl-L-aspartic acid 3-(N-(2-aminoacetamidoyl)-sulfonamido)-2,6-dichloro benzoyloxymethyl ketone;
- N-Methoxycarbonyl-L-alanine-L-aspartic acid 2,6-dichlorobenzoyloxymethyl ketone;
- N-Methoxycarbonyl glycine-L-aspartic acid 2,6-dichlorobenzoyloxymethyl ketone;
- N-Methoxycarbonyl-L-phenylalanine-L-aspartic acid 2,6-dichlorobenzoyloxy methyl ketone;
- N-Methoxycarbonyl-L-valine-L-aspartic acid 2,6-dichlorobenzoyloxymethyl ketone;
- N-Benzyloxycarbonyl-L-valine-L-aspartic acid 2,6-dichlorobenzoyloxymethyl ketone;
- N-Benzyloxycarbonyl-L-alanine-L-aspartic acid 2,6-dichlorobenzoyloxymethyl ketone;
- N-Benzyloxycarbonyl-L-valine-L-alanine-L-aspartic acid 2,6-dichlorobenzoyloxy methyl ketone;
- N-(3-Phenylpropionyl)-L-aspartic acid 2,6-dichlorobenzoyloxymethyl ketone;
- N-Methoxycarbonyl-L-aspartic acid 2,6-dichlorobenzoyloxymethyl ketone;
- N-(4-N,N-dimethylaminomethyl)benzoyl-L-aspartic acid 2,6-diclorobenzoloxy methyl ketone;
- N-Benzyloxycarbonyl-D-aspartic acid 2,6-dichlorobenzoyloxymethyl ketone;
- N-Methoxy-glycine-L-aspartic acid 2,6-dichlorobenzoyloxymethyl ketone;
- N-Methoxy-L-alanine-L-aspartic acid 2,6-dichlorobenzoyloxymethyl ketone;
- N-Methoxy-L-valine-L-aspartic acid 2,6-dichlorobenzoyloxymethyl ketone;
- N-Benzyloxy-L-valine-L-aspartic acid 2,6-dichlorobenzoyloxymethyl ketone;
- N-Benzyloxy-D-alanine-L-aspartic acid 2,6-dichlorobenzoyloxymethyl ketone;
- N-Benzyloxy-L-alanine-L-alanine-L-aspartic acid 2,6-dichlorobenzoyloxy methyl ketone;
- N-Benzyloxy-L-valine-L-alanine-L-aspartic acid 2,6-dichlorobenzoyloxy methyl ketone;
- N-Benzyloxy-D-alanine-L-alanine-L-aspartic acid 2,6-dichlorobenzoyloxy methyl ketone;
- N-(N-phenylpropionyl-valinyl-alaninyl)-3-amino-4-oxo-5-(2,6-bistrifluoro methylbenzoyloxy) pentanoic acid;
- N-(N-phenylpropionyl-valinyl-alaninyl)-3-amino-4-oxo-5-benzoyloxy pentanoic acid;
- 3-Phenylpropionyl-L-valine-L-alanine-aspartic acid 2-phenylethylcarbonyloxy

methyl ketone;

Adamantane-1-carboxylic acid 3-[2-(2-benzyloxycarbonylamino-3-methyl-butyrylamino)-propionylamino]-4-carboxy-2-oxo-butyl ester;

- 3-[2-(2-Benzyloxycarbonylamino-3-methyl-butyrylamino)-propionylamino]-5-diphenylacetoxy-4-oxo-pentanoic acid;
- 2,6-Dichloro-benzoic acid 3-(5-benzyloxycarbonylamino-naphthalene-1-sulfonylamino)-4-carboxy-2-oxo-butyl ester;

Examiner: Leigh C. Maier

Group Art Unit: 1623

- 2,6-Dichloro-benzoic acid 3-[2-(3-benzyloxycarbonylamino-phenyl)-propionylamino]-4-carboxy-2-oxo-butyl ester;
- 2,6-Dichloro-benzoic acid 3-[2-(6-benzyloxycarbonyloxy-naphthalen-2-yl)-propionylamino]-4-carboxy-2-oxo-butyl ester;
- 2,6-Dichloro-benzoic acid 3-(5-benzyloxycarbonylamino-naphthalene-1-sulfonylamino)-4-carboxy-2-oxo-butyl ester;
- 2,6-Dichloro-benzoic acid 3-[(5-benzyloxycarbonylamino-naphthalene-1-carbonyl)-amino]-4-carboxy-2-oxo-butyl ester; and
- 2,6-Dichloro-benzoic acid 3-[(4-benzyloxycarbonylamino-cyclohexanecarbonyl)-amino]-4-carboxy-2-oxo-butyl ester.
- 2. (Original) A compound according to Claim 1 wherein R<sup>1</sup> is

- 3. (Original) A compound according to Claim 1 wherein R<sup>1</sup> is phenyl-SO<sub>2</sub>—.
- 4. (Original) A compound according to Claim 1 wherein R<sup>1</sup> is

$$H_3C-OC-$$

5. (Original) A compound according to Claim 1 wherein R<sup>1</sup> is phenyl-CH<sub>2</sub>CH<sub>2</sub>-CO—.

6. (Original) A compound according to Claim 1 wherein R<sup>1</sup> is

$$H_3C$$
  $NH$   $CH_3$ 

7. (Original) A compound according to Claim 1 wherein R<sup>1</sup> is

8. (Original) A compound according to Claim 1 wherein R<sup>1</sup> is phenyl-CH<sub>2</sub>-CO—

Examiner: Leigh C. Maier

- 9. (Previously Cancelled).
- 10. (Original) A compound according to Claim 1 wherein each Ra is hydrogen.
- 11. (Original) A compound according to Claim 1 wherein  $R^2$  is — $(CH_2)_n$ -phenyl.
- 12. (Original) A compound according to Claim 1 wherein  $R^2$  is  $(CH_2)_n$ -naphthyl.
- 13. (Original) A compound according to Claim 1 wherein  $R^2$  is  $(CH_2)_n$ -O-phenyl.
- (Original) A compound according to Claim 1 wherein R<sup>2</sup> is —(CH<sub>2</sub>)<sub>n</sub>-O-naphthyl.
- 15. (Original) A compound according to Claim 1 wherein  $R^2$  is — $(CH_2)_n$ -S-phenyl.
- (Original) A compound according to Claim 1 wherein R<sup>2</sup> is—(CH<sub>2</sub>)<sub>n</sub>-CH(phenyl)<sub>2</sub>.
- 17. (**Previously Amended**) A compound according to Claim 1 wherein each R<sup>a</sup> is hydrogen; R<sup>1</sup> is benzyloxycarbonyl; R<sup>2</sup> is aryl-X(CRR)<sub>n</sub>—, aryl-(CRR)<sub>n</sub>—, or cycloalkyl-(CRR)<sub>n</sub>—; n is 1, 2, or 3; X is O or S; and R is hydrogen, methyl, or benzyl.
- 18. (Previously Amended) A compound according to Claim 1 wherein each Ra is hydrogen;

Examiner: Leigh C. Maier Group Art Unit: 1623

Rí is benzyloxycarbonyl; and

$$R^2$$
 is — $(CH_2)_n$ -naphthyl,

- $-(CH_2)_n$ -phenyl,
- --(CH<sub>2</sub>)<sub>n</sub>-cycloalkyl,
- $--(CH_2)_nO(CH_2)_n$ -naphthyl,
- $--(CH_2)_nO(CH_2)_n$ -phenyl, or
- $-(CH_2)_nS(CH_2)_n$ -phenyl.
- 19. (Original) A compound according to Claim 1 wherein each Ra is hydrogen;

R1 is benzyloxycarbonyl; and

 $R^2$  is — $CH_2$ -naphthyl.

20. (Previously Amended) A compound in accordance with Claim 1

wherein each Ra is hydrogen; and

R<sup>1</sup> is benzyloxycarbonyl,

$$\begin{array}{c} O \\ -\overset{\parallel}{\text{S}} \\ O \\ O \\ -\overset{\parallel}{\text{C}} \\ -\overset{\overset{\parallel}{\text{C}} \\ -\overset{\overset{\parallel}{\text{C}} \\ -\overset{\overset{\parallel}{\text{C}} \\ -\overset{\overset{\parallel}{\text{C}} \\ -\overset{\overset{\parallel}{\text{C}} \\ -\overset{\overset{\parallel}{\text{C}} \\ -\overset{\overset{\parallel}{\text{C}}$$

$$\begin{array}{ccc} O & O \\ \parallel & \parallel \\ -C - CH - CH_2 - S - aryl \\ CH_3 & O \end{array}$$

21. (Original) A method of inhibiting interleukin-1β converting enzyme, the method comprising administering to a patient in need of inhibition of interleukin-1β converting enzyme a therapeutically effective amount of a compound of Claim 1.

Examiner: Leigh C. Maier

- 22. (**Original**) A method of inhibiting Caspase-4, the method comprising administering to a patient in need of inhibition of Caspase-4 inhibition a Caspase-4 inhibiting amount of a compound of Claim 1.
- 23. (**Original**) A method of treating stroke, the method comprising administering to a patient having a stroke or having had a stroke a therapeutically effective amount of a compound of Claim 1.
- 24. (**Original**) A method of treating inflammatory diseases, the method comprising administering to a patient having an inflammatory disease a therapeutically effective amount of a compound of Claim 1.
- 25. (Original) The method of Claim 24 wherein the inflammatory disease is arthritis.
- 26. (**Original**) The method of Claim 24 wherein the inflammatory disease inflammatory bowel disease.
- 27. (**Original**) A method of treating reperfusion injury, the method of comprising administering to a patient having reperfusion injury a therapeutically effective amount of a compound of Claim 1.
- 28. (Original) A method of treating Alzheimer's disease, the method comprising administering to a patient having Alzheimer's disease a therapeutically effective amount of a compound of Claim 1.
- 29. (Original) A method of treating shigellosis, the method comprising administering to a patient having shigellosis a therapeutically effective amount of a compound of Claim 1.

30. (**Original**) A pharmaceutically acceptable composition that contains a compound of Claim 1.

Examiner: Leigh C. Maier

- 31. (Previously Cancelled).
- 32. (Previously Cancelled).
- 33. (Previously Cancelled).
- 34. (Previously Amended) The compounds:
  - (S)-5-(Naphthalene-1-yl-acetoxy)-4-oxo-3-phenylacetylamino-pentanoic acid;
  - 3-[(2-Carbamoyl-cyclopentanecarbonyl)-amino]-5-(naphthalen-1-yl-acetoxy)-4-oxopentanoic acid;
  - 3-[(3-Carbamoyl-bicyclo[2.2.1]heptane-2-carbonyl)-amino]-5-(naphthalen-1-yl-acetoxy)-4-oxo-pentanoic acid;
  - 3-(3-Methanesulfonyl-2-methyl-propionylamino)-5-(naphthalen-1-yl-acetoxy)-4-oxopentanoic acid;
  - 3-(3-Benzenesulfonyl-2-methyl-propionylamino)-5-(naphthalen-1-yl-acetoxy)-4-oxopentanoic acid;
  - 3-Butyrylamino-5-(naphthalen-2-yl-acetoxy)-4-oxo-pentanoic acid;
  - 3-Acetylamino-5-(naphthalen-1-yl-acetoxy)-4-oxo-pentanoic acid;
  - 3-(3-Methanesulfonyl-2-methyl-propionylamino)-5-(naphthalen-1-yl-acetoxy)-4-oxopentanoic acid;
  - 3-(3-Methyl-butyrylamino)-5-(naphthalen-1-yl-acetoxy)-4-oxo-pentanoic acid;
  - 3-(3-Carbamoyl-propionylamino)-5-(naphthalen-1-yl-acetoxy)-4-oxo-pentanoic acid;
  - [S-(R\*,R\*)]-3-(3-Acetylsulfanyl-2-methyl-propionylamino)-5-(naphthalen-1-yl-acetoxy)-4-oxo-pentanoic acid; and
  - *trans*-3-[(3-Carbamoyl-cyclopentanecarbonyl)-amino]-5-(naphthalen-1-yl-acetoxy)-4-oxopentanoic acid.
- 35. (Previously Cancelled).
- 36. (Previously Cancelled).
- 37. (Previously Cancelled).

# 38. (Original) The compounds:

3-[(2-Carboxy-cyclohexanecarbonyl)-amino]-5-(naphthalen-1-yl-acetoxy)-4-oxopentanoic acid;

Examiner: Leigh C. Maier

Group Art Unit: 1623

- 3-[(2-Methoxycarbonyl-cyclohexanecarbonyl)-amino]-5-(naphthalen-1-yl-acetoxy)-4-oxo-pentanoic acid; and
- 3-[(2-Carbamoyl-cyclohexanecarbonyl)-amino]-5-(naphthalen-1-yl-acetoxy)-4-oxopentanoic acid.

## 39. (Original) The compounds:

- 3-(3-Benzylsulfanyl-2-methyl-propionylamino)-5-(naphthalen-1-yl-acetoxy)-4-oxopentanoic acid;
- 3-(2-Methyl-3-phenylmethanesulfonyl-propionylamino)-5-(naphthalen-1-yl-acetoxy)-4-oxo-pentanoic acid;
- 3-[3-(2-Carboxy-ethanesulfanyl)-2-methyl-propionylamino]-5-(naphthalen-1-yl-acetoxy)-4-oxo-pentanoic acid;
- 5-(2-Benzyl-3-phenyl-propionyloxy)-3-[3-(2-carboxy-ethanesulfonyl)-2-methyl-propionyl amino]-4-oxo-pentanoic acid;
- 5-(2-Benzyl-3-phenyl-propionyloxy)-3-[3-(3-carboxy-propane-1-sulfinyl)-2-methyl-propionylamino]-4-oxo-pentanoic acid;
- 5-(Naphthalen-1-yl-acetoxy)-4-oxo-3-(2-phenylmethanesulfanyl-propionylamino)-pentanoic acid;
- 3-(2-Methyl-3-phenylsulfanyl-propionylamino)-5-(naphthalen-1-yl-acetoxy)-4-oxopentanoic acid;
- 5-(2-Benzyl-3-phenyl-propionyloxy)-3-(2-methyl-3-phenylsulfanyl-propionylamino)-4-oxo-pentanoic acid;
- 3-(2-Methyl-3-phenethylsulfanyl-propionylamino)-5-(naphthalen-1-yl-acetoxy)-4-oxopentanoic acid;
- 5-(2-Benzyl-3-phenyl-propionyloxy)-3-(2-methyl-3-phenethylsulfanyl-propionylamino)-4-oxo-pentanoic acid;
- 5-(2-Benzyl-3-phenyl-propionyloxy)-3-(3-benzylsulfanyl-2-methyl-propionylamino)-4-oxo-pentanoic acid;
- 5-(2-Benzyl-3-phenyl-propionyloxy)-3-(2-benzylsulfanyl-propionylamino)-4-oxopentanoic acid;
- 3-[2-Methyl-3-(3-phenyl-propylsulfanyl)-propionylamino]-5-(naphthalen-1-yl-acetoxy)-4-oxo-pentanoic acid;

'3-(3-Benzenesulfonyl-2-methyl-propionylamino)-5-(naphthalen-1-yl-acetoxy)-4-oxopentanoic acid;

Examiner: Leigh C. Maier

- 3-(3-Benzenesulfonyl-2-methyl-propionylamino)-5-(2-benzyl-3-phenyl-propionyloxy)-4-oxo-pentanoic acid;
- 5-(2-Benzyl-3-phenyl-propionyloxy)-3-[2-methyl-3-(2-phenyl-ethanesulfonyl)-propionyl amino]-4-oxo-pentanoic acid;
- 3-[2-Methyl-3-(2-phenyl-ethanesulfonyl)-propionylamino]-5-(naphthalen-1-yl-acetoxy)-4-oxo-pentanoic acid;
- 5-(Naphthalen-1-yl-acetoxy)-4-oxo-3-(2-phenylmethanesulfonyl-propionylamino)-pentanoic acid;
- 5-(2-Benzyl-3-phenyl-propionyloxy)-3-(2-methyl-3-phenylmethanesulfonyl-propionyl amino)-4-oxo-pentanoic acid;
- 5-(2-Benzyl-3-phenyl-propionyloxy)-4-oxo-3-(2-phenylmethanesulfonyl-propionylamino)-pentanoic acid;
- 3-[2-Methyl-3-(3-phenyl-propane-1-sulfonyl)-propionylamino]-5-(naphthalen-1-yl-acetoxy)-4-oxo-pentanoic acid;
- 5-(2-Benzyl-3-phenyl-propionyloxy)-3-[2-methyl-3-(3-phenyl-propane-1-sulfonyl)-propionylamino]-4-oxo-pentanoic acid;
- 5-(2-Benzyl-3-phenyl-propionyloxy)-3-[3-(2-carboxy-ethylsulfanyl)-2-methyl-propionyl amino]-4-oxo-pentanoic acid;
- 3-[3-(3-Carboxy-propylsulfanyl)-2-methyl-propionylamino]-5-(naphthalen-1-yl-acetoxy)-4-oxo-pentanoic acid;
- 5-(2-Benzyl-3-phenyl-propionyloxy)-3-[3-(3-carboxy-propylsulfanyl)-2-methyl-propionyl amino]-4-oxo-pentanoic acid;
- 3-(3-Carboxymethylsulfanyl-2-methyl-propionylamino)-5-(naphthalen-1-yl-acetoxy)-4-oxo-pentanoic acid;
- 5-(2-Benzyl-3-phenyl-propionyloxy)-3-(3-carboxymethylsulfanyl-2-methyl-propionyl amino)-4-oxo-pentanoic acid;
- 3-[3-(2-Carboxy-ethanesulfonyl)-2-methyl-propionylamino]-5-(naphthalen-1-yl-acetoxy)-4-oxo-pentanoic acid;
- 3-[3-(3-Carboxy-propane-1-sulfonyl)-2-methyl-propionylamino]-5-(naphthalen-1-yl-acetoxy)-4-oxo-pentanoic acid;
- 3-(3-Carboxymethanesulfonyl-2-methyl-propionylamino)-5-(naphthalen-1-yl-acetoxy)-4-oxo-pentanoic acid;

5-(2-Benzyl-3-phenyl-propionyloxy)-3-[3-(3-carboxy-propane-1-sulfonyl)-2-methyl propionylamino]-4-oxo-pentanoic acid;

Examiner: Leigh C. Maier

Group Art Unit: 1623

- 5-(2-Benzyl-3-phenyl-propionyloxy)-3-(3-carboxymethanesulfonyl-2-methyl-propionyl amino)-4-oxo-pentanoic acid;
- 3-[3-(3-Carboxy-propane-1-sulfinyl)-2-methyl-propionylamino]-5-(naphthalen-1-yl-acetoxy)-4-oxo-pentanoic acid;
- 3-[2-Methyl-3-(3-phenyl-propane-1-sulfinyl)-propionylamino]-5-(naphthalen-1-yl-acetoxy)-4-oxo-pentanoic acid; and
- 5-(2-Benzyl-3-phenyl-propionyloxy)-3-[2-methyl-3-(3-phenyl-propane-1-sulfinyl)-propionylamino]-4-oxo-pentanoic acid.

### 40. (Original) The compounds:

- 3-[3-Methyl-2-(phenethylcarbamoyl-methyl)-butyrylamino]-5-(naphthalen-1-yl-acetoxy)-4-oxo-pentanoic acid; and
- 3-(3-Carboxy-2-methyl-propionylamino)-5-(naphthalen-1-yl-acetoxy)-4-oxopentanoic acid.

## 41. (Original) The compound:

3-(2-Methyl-3-sulfamoyl-propionylamino)-5-(naphthalen-1-yl-acetoxy)-4-oxopentanoic acid.

#### 42. (Previously Cancelled).

### 43. (Previously Cancelled).

- 3-Benzyloxycarbonylamino-5-(naphthalen-1-yl-acetoxy)-4-oxo-pentanoic acid;
- 3-Benzyloxycarbonylamino-4-oxo-5-(3-phenyl-propionyloxy)-pentanoic acid;
- 3-Benzyloxycarbonylamino-5-(3-cyclohexyl-propionyloxy)-4-oxo-pentanoic acid;
- 3-Benzyloxycarbonylamino-5-[(naphthalene-1-yl-oxy)-acetoxy]-4-oxo-pentanoic acid;
- 3-Benzyloxycarbonylamino-4-oxo-5-phenoxyacetoxy-pentanoic acid;
- 3-Benzyloxycarbonylamino-4-oxo-5-phenylsulfanylacetoxy-pentanoic acid;
- 3-Benzyloxycarbonylamino-5-[(6-methoxy-naphthalene-1-yl)-acetoxy]-4-oxopentanoic acid;
- 3-Benzyloxycarbonylamino-5-(naphthalene-2-yl-acetoxy)-4-oxo-pentanoic acid;
- 3-Benzyloxycarbonylamino-5-(3-naphthalene-2-yl-propionyloxy)-4-oxo-pentanoic acid;

- 3-Benzyloxycarbonylamino-5-(3,3-diphenyl-propionyloxy)-4-oxo-pentanoic acid;
- 3-Benzyloxycarbonylamino-5-(2-naphthalene-1-yl-propionyloxy)-4-oxo-pentanoic acid;

- 5-[(Acetyl-phenyl-amino)-acetoxy]-3-benzyloxycarbonyl-amino-4-oxo-pentanoic acid;
- 3-Benzyloxycarbonylamino-5-(2-benzyl-3-phenyl-propionyloxy)-4-oxo-pentanoic acid;
- 3-Benzyloxycarbonylamino-5-(hydroxy-naphthalene-1-yl-acetoxy)-4-oxo-pentanoic acid;
- 3-Benzyloxycarbonylamino-4-oxo-5-[(phenyl-amino)-acetoxy]-pentanoic acid;
- 3-Benzyloxycarbonylamino-5-[(6-hydroxy-naphthalene-1-yl)-acetoxy]-4-oxopentanoic acid;
- 3-Benzyloxycarbonylamino-5-[3-(4-hydroxy-phenyl)-2-naphthalene-1-yl-propionyloxy)-4-oxo-pentanoic acid;
- (S)-3-Benzyloxycarbonylamino-4-oxo-5-phenylacetoxy-pentanoic acid;
- (S)-3-Benzyloxycarbonylamino-4-oxo-5-(4-phenyl-butyryloxy)-pentanoic acid;
- 3-Benzyloxycarbonylamino-4-oxo-5-[(4-phenyl-naphthalen-1-yl)-acetoxy]-pentanoic acid;
- 3-Benzyloxycarbonylamino-5-[(4-methyl-naphthalen-1-yl)-acetoxy]-4-oxo-pentanoic acid;
- 3-Benzyloxycarbonylamino-4-oxo-5-[(4-thiophen-2-yl-naphthalen-1-yl)-acetoxy]-pentanoic acid;
- 3-Benzyloxycarbonylamino-5-[(4-fluoro-naphthalen-1-yl)-acetoxy]-4-oxo-pentanoic acid;
- 3-Benzyloxycarbonylamino-5-[(2-methyl-naphthalen-1-yl)-acetoxy]-4-oxo-pentanoic acid;
- 3-Benzyloxycarbonylamino-5-[(2-fluoro-naphthalen-1-yl)-acetoxy]-4-oxo-pentanoic acid;
- 5-[(4-Benzyl-naphthalen-1-yl)-acetoxy]-3-benzyloxycarbonylamino-4-oxo-pentanoic acid;
- 3-Benzyloxycarbonylamino-5-[(3,4-dihydro-naphthalen-1-yl)-acetoxy]-4-oxopentanoic acid;
- 3-Benzyloxycarbonylamino-5-(3,4-diphenyl-butyryloxy)-4-oxo-pentanoic acid;
- 3-Benzyloxycarbonylamino-4-oxo-5-(3-phenyl-3-phenylamino-propionyloxy)-pentanoic acid;
- 3-Benzyloxycarbonylamino-4-oxo-5-[(1,2,3,4-tetrahydro-naphthalen-2-yl)-acetoxy]-pentanoic acid;
- 3-Benzyloxycarbonylamino-4-oxo-5-[(2,3,5,6-tetramethyl-phenyl)-acetoxy]-pentanoic acid;
- 3-Benzyloxycarbonylamino-5-[(2,3-dichloro-phenyl)-acetoxy]-4-oxo-pentanoic acid;
- 3-Benzyloxycarbonylamino-5-[(5-methyl-naphthalen-1-yl)-acetoxy]-4-oxo-pentanoic acid;
- 3-Benzyloxycarbonylamino-5-[(2-iodo-phenyl)-acetoxy]-4-oxo-pentanoic acid;
- 3-Benzyloxycarbonylamino-5-[(5-methoxy-naphthalen-1-yl)-acetoxy]-4-oxopentanoic acid;
- $3-Benzyloxy carbonylamino-5-[(8-methyl-naphthalen-1-yl)-acetoxy]-4-oxo-pentanoic\ acid;$

- 3-Benzyloxycarbonylamino-5-[(9H-fluoren-9-yl)-acetoxy]-4-oxo-pentanoic acid;
- 3-Benzyloxycarbonylamino-5-[(10,11-dihydro-5H-dibenzo[a,d]cyclohepten-5-yl)-acetoxy]-4-oxo-pentanoic acid;
- 3-Benzyloxycarbonylamino-5-(2-benzyl-3-phenyl-propionyloxy)-4-oxo-pentanoic acid; and

Group Art Unit: 1623

3-Benzyloxycarbonylamino-5-[(5-cyano-naphthalen-1-yl)-acetoxy]-4-oxo-pentanoic acid.

## 45. (Previously Added) The compounds:

- [S-(R\*,R\*)]-3-(2-Acetylamino-propionylamino)-5-(naphthalene-1-yl-acetoxy)-4-oxopentanoic acid;
- 5-(Naphthalen-1-yl-acetoxy)-4-oxo-3-[(thiophene-3-carbonyl)-amino]-pentanoic acid;
- 3-(2-Methanesulfonylamino-propionylamino)-5-(naphthalen-1-yl-acetoxy)-4-oxopentanoic acid;
- 3-[2-(2-Acetylamino-4-phenyl-butyrylamino)-propionylamino]-5-(naphthalen-1-yl-acetoxy)-4-oxo-pentanoic acid;
- 3-(2-Acetylamino-butyrylamino)-5-(naphthalen-1-yl-acetoxy)-4-oxo-pentanoic acid;
- 3-[2-(4-Carbamoyl-butyrylamino)-propionylamino]-5-(naphthalen-1-yl-acetoxy)-4-oxo-pentanoic acid;
- 3-(2-Benzyloxycarbonylamino-propionylamino)-5-(naphthalen-1-yl-acetoxy)-4-oxopentanoic acid;
- 5-(Naphthalen-1-yl-acetoxy)-4-oxo-3-(2-ureido-propionylamino)-pentanoic acid;
- 3-(2-Acetylamino-propionylamino)-5-(naphthalen-1-yl-acetoxy)-4-oxo-pentanoic acid;
- 3-(2-Acetylamino-acetylamino)-5-(naphthalen-1-yl-acetoxy)-4-oxo-pentanoic acid;
- 3-(2-Acetylamino-propionylamino)-5-(3,3-diphenyl-propionyloxy)-4-oxo-pentanoic acid;
- 3-[2-(2-Acetylamino-4-carboxy-butyrylamino)-propionylamino]-5-(naphthalen-1-yl-acetoxy)-4-oxo-pentanoic acid;
- 5-(Naphthalen-1-yl-acetoxy)-4-oxo-3-[2-(3-phenyl-propionylamino)-propionylamino]-pentanoic acid;
- 3-[2-(3-Methyl-butyrylamino)-propionylamino]-5-(naphthalen-1-yl-acetoxy)-4-oxopentanoic acid; and
- 3-(4-Carbamoyl-butyrylamino)-5-(naphthalen-1-yl-acetoxy)-4-oxo-pentanoic acid.

- 3-(2-Methyl-3-phenethylcarbamoyl-propionylamino)-5-(naphthalen-1-yl-acetoxy)-4-oxopentanoic acid;
- 3-[3-Methyl-2-(3-phenyl-propionylamino)-butyrylamino]-4-oxo-5-[(1-oxo-

- 1,2,3,4-tetrahydro-naphthalen-2-yl)-acetoxy]-pentanoic acid;
- 5-(Naphthalen-2-yl-acetoxy)-4-oxo-3-[2-(1-oxo-3,4-dihydro-1H-isoquinolin-2-yl)-acetylamino]-pentanoic acid;
- 5-(2-Benzyl-3-phenyl-propionyloxy)-4-oxo-3-[2-(1-oxo-1,2,3,4-tetrahydro-naphthalen-2-yl)-acetylamino]-pentanoic acid;

Group Art Unit: 1623

- 4-Oxo-5-[(1-oxo-1,2,3,4-tetrahydro-naphthalen-2-yl)-acetoxy]-3-[2-(1-oxo-1,2,3,4-tetrahydro-naphthalen-2-yl)-acetylamino]-pentanoic acid;
- 3-(2-Acetylamino-3-methyl-butyrylamino)-5-(naphthalen-1-yl-acetoxy)-4-oxopentanoic acid;
- 3-(2-Acetylamino-3-methyl-butyrylamino)-5-(2-benzyl-3-phenyl-propionyloxy)-4-oxopentanoic acid;
- 3-(2-Acetylamino-3-methyl-butyrylamino)-5-(3-benzyl-4-phenyl-butyryloxy)-4-oxopentanoic acid;
- 3-(2-Acetylamino-3-methyl-butyrylamino)-5-(4-benzyl-5-phenyl-pentanoyloxy)-4-oxopentanoic acid;
- 3-(2-Acetylamino-3-methyl-butyrylamino)-4-oxo-5-[(1-oxo-1,2,3,4-tetrahydro naphthalen-2-yl)-acetoxy]-pentanoic acid; and
- 5-(3-Benzyl-4-phenyl-butyryloxy)-3-[3-methyl-2-(3-phenyl-propionylamino)-butyrylamino]-4-oxo-pentanoic acid.

- 3-[2-(2-Benzyloxycarbonylamino-4-carboxy-butyrylamino)-3-methyl-butyrylamino]-5-(naphthalen-1-yl-acetoxy)-4-oxo-pentanoic acid;
- 3-[2-(2-Benzyloxycarbonylamino-3-methyl-butyrylamino)-propionylamino]-5-(naphthalen-1-yl-acetoxy)-4-oxo-pentanoic acid;
- 3-(2-Acetylamino-3-methyl-butyrylamino)-5-(naphthalen-1-yl-acetoxy)-4-oxopentanoic acid;
- 3-[2-(2-Benzyloxycarbonylamino-3-methyl-butyrylamino)-propionylamino]-5-(3,3-diphenyl-propionyloxy)-4-oxo-pentanoic acid;
- 3-[2-(2-Benzyloxycarbonylamino-3-methyl-butyrylamino)-propionylamino]-5-(2-benzyl-3-phenyl-propionyloxy)-4-oxo-pentanoic acid;
- 3-[2-(2-Benzyloxycarbonylamino-3-methyl-butyrylamino)-propionylamino]-5-(naphthalen-1-yl-acetoxy)-4-oxo-pentanoic acid;
- 5-(2-Benzyl-3-phenyl-propionyloxy)-3-{2-[4-carboxy-2-(3-phenyl-propionyl amino)-butyrylamino]-3-methyl-butyrylamino}-4-oxo-pentanoic acid;

- 3-(2-Benzyloxycarbonylamino-3-methyl-butyrylamino)-5-(3,3-diphenyl-propionyloxy)-4-oxo-pentanoic acid;
- 3-(2-Acetylamino-3-hydroxy-butyrylamino)-5-(naphthalen-1-yl-acetoxy)-4-oxopentanoic acid;

Group Art Unit: 1623

- 3-(2-Acetylamino-3-hydroxy-butyrylamino)-5-(3,3-diphenyl-propionyloxy)-4-oxopentanoic acid; and
- 5-(3,3-Diphenyl-propionyloxy)-4-oxo-3-[2-(4-phenyl-butyrylamino)-propionyl aminol-pentanoic acid.

## 48. (Previously Added) The compounds:

3-(2-{2-[2-Acetylamino-3-(4-hydroxy-phenyl)-propionylamino]-4-carboxy-butyrylamino}-3-methyl-butyrylamino)-5-(naphthalen-1-yl-acetoxy)-4-oxo-pentanoic acid.

- 3-(3-Carbamoyl-2-methyl-propionylamino)-5-(naphthalen-1-yl-acetoxy)-4-oxopentanoic acid;
- 3-(2-Benzyloxycarbonylamino-3-methyl-naphthalen-1-yl-acetoxy)-4-oxo-pentanoic acid;
- 3-[(2-Carbamoyl-cyclopentanecarbonyl)-amino]-5-(naphthalen-1-yl-acetoxy)-4-oxopentanoic acid;
- 3-(2-{2-[2-Acetylamino-3-(4-hydroxy-phenyl)-propionylamino]-4-carboxy-butyrylamino}-3-methyl-butyrylamino)-5-(2-benzyl-3-phenyl-propionyloxy)-4-oxo-pentanoic acid;
- 3-(3-Carbamoyl-2-methyl-propionylamino)-5-(naphthalen-1-yl-acetoxy)-4-oxopentanoic acid;
- 3-(2-Carbamoylmethyl-3-methyl-butyrylamino)-5-(naphthalen-1-yl-acetoxy)-4-oxopentanoic acid;
- 3-(3-Benzyloxy-2-ureido-propionylamino)-5-(naphthalen-1-yl-acetoxy)-4-oxopentanoic acid;
- 3-[2-(2-Benzyloxycarbonylamino-4-carboxy-butyrylamino)-3-methyl-butyrylamino]-5-(2-benzyl-3-phenyl-propionyloxy)-4-oxo-pentanoic acid;
- 3-{2-[4-Carboxy-2-(3-phenyl-propionylamino)-butyrylamino]-3-methyl-butyrylamino}-5-(naphthalen-1-yl-acetoxy)-4-oxo-pentanoic acid; and
- 3-[2-(2-Acetylamino-4-carboxy-butyrylamino)-3-methyl-butyrylamino]-5-(naphthalen-1-yl-acetoxy)-4-oxo-pentanoic acid.

# 50. (Currently Amended) A compound of the Formula I

I

Examiner: Leigh C. Maier

Group Art Unit: 1623

wherein R1 is

$$\begin{array}{c} {\rm O} \\ {\rm II} \\ {\rm --COCH_2~phenyl_,} \end{array}$$

$$\begin{array}{c} O \\ -II \\ -CCH_2 \text{ thienyl}, \end{array}$$

$$-^{\mathrm{O}}_{\mathrm{CC_1-C_6}}$$
 alkyl,

$$\begin{array}{c} O \\ \parallel \\ --C-CH-SCH_2-phenyl \\ l \\ CH_3 \end{array},$$

$$\begin{array}{c|c} O & O & O \\ \hline -C & -CH - NHC - CH - NHCOCH_2 phenyl \\ \hline H_3C & CH_3 & (CH_2)_2 \\ \hline & CO_2H \end{array}$$

$$-\overset{O}{\overset{\square}{\text{C}}}-\text{NH}_2$$

$$\begin{array}{c} \text{O} \\ \text{---}\text{C}\text{--}\text{CH--}\text{CH}_2\text{S--phenyl} \\ \text{CH}_3 \end{array},$$

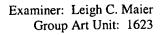
$$\begin{array}{ccc} O & O \\ \parallel & \parallel \\ --C-CH-CH_2S-phenyl \\ CH_3 & O \end{array}$$

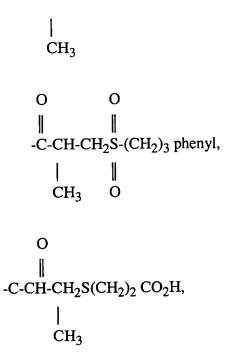
$$\begin{array}{c} \text{O} \\ \text{---}\text{C}\text{--}\text{CH--}\text{CH}_2\text{S--}(\text{CH}_2)_2\text{--phenyl} \\ \text{CH}_3 \end{array}$$

$$\begin{array}{cccc} O & O \\ \parallel & \parallel \\ --C-CH-CH_2S-(CH_2)_2-phenyl \\ \parallel & \parallel \\ CH_3 & O \end{array},$$

$$\begin{array}{ccc} O & O \\ \parallel & \parallel \\ --C-CH-CH_2S-(CH_2)_2-phenyl \\ \downarrow & \parallel \\ CH_3 & O \end{array}$$

$$\begin{array}{cccc} O & O \\ \parallel & \parallel \\ -C-CH-S-CH_2 \text{ phenyl} \\ CH_3 \overset{\circ}{O} \end{array}$$





O O 
$$\parallel$$
  $\parallel$   $\parallel$  -C-CHCH<sub>2</sub>S(CH<sub>2</sub>)<sub>2</sub>CO<sub>2</sub>H, or  $\parallel$   $\parallel$  CH<sub>3</sub> O

Group Art Unit: 1623

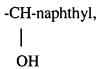
O 
$$\parallel$$
 -CCHCH<sub>2</sub>S-(CH<sub>2</sub>)<sub>2</sub>CO<sub>2</sub>H; and  $\parallel$  CH<sub>3</sub> O

 $R^2$  is

- -CH<sub>2</sub>CH<sub>2</sub> phenyl,
- -CH<sub>2</sub> naphthyl,
- -CH<sub>2</sub>CH<sub>2</sub> cyclohexyl,
- -CH<sub>2</sub>O naphthyl,
- -CH<sub>2</sub>O phenyl,
- -CH<sub>2</sub>S-phenyl,
- -CH<sub>2</sub>-substituted naphthyl,
- - $CH_2CH(phenyl)_2$ ,
- -(CH<sub>2</sub>)<sub>3</sub>-phenyl,
- -CH-naphthyl,

$$CH_3$$
 $CH_2$ 
 $O$ 
 $CH_2$ 
 $O$ 

-CH[CH<sub>2</sub>phenyl]<sub>2</sub>,



-CH<sub>2</sub>-NH phenyl,

$$-\underbrace{\mathrm{CH_2}}^{\mathrm{CH_2} \mathrm{substituted\ phenyl}}_{\mathrm{naphthyl}},$$

Examiner: Leigh C. Maier

Group Art Unit: 1623

-CH<sub>2</sub>-naphthyl-phenyl,

-CH<sub>2</sub>-fluorenyl,

-CH<sub>2</sub>-naphthyl-CH<sub>2</sub> phenyl,

-CH<sub>2</sub>-substituted phenyl,

$$-CH_2$$

$$-CH_2$$

Application No. 09/284,424, filed 9 April 1999 Amendment and Response of 23 October 2003 Responsive to Office Action of 23 April 2003

$$-CH_2$$
, or  $-CH_2$ 

each n is independently 0 to 3, and the pharmaceutically acceptable, salts, esters, amides, and prodrugs thereof.

Examiner: Leigh C. Maier

Group Art Unit: 1623

### 51. (Previously Added) The compounds:

- 3-Benzenesulfonylamino-5-(naphthalen-1-yl-acetoxy)-4-oxo-pentanoic acid;
- 3-Methoxycarbonylamino-5-(naphthalene-1-yl-acetoxy)-4-oxo-pentanoic acid;
- 5-(Naphthalene-1-yl-acetoxy)-4-oxo-3-(3-phenyl-propionylamino)-pentanoic acid;
- 3-Methoxycarbonylamino-4-oxo-5-phenoxyacetoxy-pentanoic acid; and
- 3-(2-Methanesulfonyl-1-methyl-ethylsulfanylamino)-5-(naphthalen-1-yl-acetoxy)-4-oxo-pentanoic acid.

### 52. (Currently Amended) A compound of the Formula I

wherein R<sup>1</sup> is

each Ra is independently hydrogen, C1-C6 alkyl, or -(CH2)n aryl;

 $R^2$  is  $--(CRR)_n$ -aryl,

 $--(CRR)_n$ -X-aryl,

 $-(CRR)_n$ -(substituted-aryl), provided that the aryl group is not substituted with alkoxy, halogen, or trifluoromethyl,

Examiner: Leigh C. Maier

- —(CRR)<sub>n</sub>-X-(substituted-aryl),
- --(CRR)<sub>n</sub>-aryl-aryl,
- $--(CRR)_n$ -aryl- $(CH_2)_n$ -aryl,
- $--(CRR)_n$ -CH(aryl)<sub>2</sub>,
- $--CRR)_n$ -cycloalkyl,
- --(CRR)<sub>n</sub>-X-cycloalkyl,

$$-(CRR)_n$$
  $-CH$   $(CH_2)_n$   $-aryl$   $(CH_2)_n$   $-aryl$  ,

$$-(CRR)_n$$
 —  $CH_2$   $n$  — substituted aryl  $(CH_2)_n$  —  $aryl$ 

$$-(CRR)_n$$

$$-(CRR)_n$$

$$-(CRR)_n$$

Group Art Unit: 1623

each R is independently hydrogen, C<sub>1</sub>-C<sub>6</sub> alkyl, halogen or hydroxy;

X is O or S;

$$R^3$$
 is  $C_1$ - $C_6$  alkyl,

—(CHR)<sub>n</sub>-substituted aryl,

$$-(CRR)_n$$
 $-C$  $-OR^a$ 

$$-(CRR)_nO(CH_2)_n$$
-aryl,

cycloalkyl,

substituted cycloalkyl,

$$-(CRR)_n-\overset{O}{C}-NR^aR^a$$

$$O$$
 $\parallel$ 
 $-(CH_2)_nNHCC_1-C_6$  alkyl

$$-(CH_2)_nCNR^bR^b$$

each R' is independently C1-C6 alkyl,

C<sub>1</sub>-C<sub>6</sub> alkylaryl,

aryl, or

hydrogen;

each J is independently

- $-CO_2R^b$ ,
- -CONRbRb,
- -SO<sub>2</sub>NR<sup>b</sup>R<sup>b</sup>, or
- $-SO_2R^b$ ;

each R<sup>b</sup> is independently hydrogen, C<sub>1</sub>-C<sub>6</sub> alkyl, aryl, substituted aryl, arylalkyl, or substituted arylalkyl;

Examiner: Leigh C. Maier

Group Art Unit: 1623

R<sup>4</sup> is hydrogen,

$$C_1$$
- $C_6$  alkyl,

$$H_3CO-C$$

---phenyl, or

Examiner: Leigh C. Maier

Group Art Unit: 1623

$$C_1$$
- $C_6$  alkyl- $C$ -,

$$R^5$$
 is  $C_1$ - $C_6$  alkyl- $CO$ —,

$$C_1$$
- $C_6$  alkylO- $C$ -

$$C_1$$
- $C_6$ -alkyl- $X$ - $(CH_2)_nCO$ ,

$$C_1$$
- $C_6$  alkyl- $X$ - $(CH_2)_nO$ - $C$ -

$$-\frac{O}{C(CRR)_n}$$
 aryl,

$$\begin{array}{c} O \\ II \\ --SC_1-C_6 \text{ alkyl} \\ O \end{array}$$

$$\begin{array}{ccc} O & O \\ \parallel & \parallel \\ --C(CH_2)_nCNR^aR^a \end{array}$$

$${\displaystyle \mathop{-}^{\scriptstyle O}_{\scriptstyle II}}_{\scriptstyle CO(CH_2)_n \; aryl},$$

$$\begin{array}{c} O \\ II \\ --CO(CH_2)_n \end{array}$$
 substituted aryl

$$\begin{array}{ccc} O & O \\ II & II \\ --C(CRR)_nNHCO(CH_2)_n-aryl \end{array},$$

$$-\overset{O}{\underset{R^{6}}{\parallel}}-\overset{R^{a}}{\underset{R^{5a}}{\parallel}}$$

$$--(CH_2)_nX(CH_2)_n$$
-aryl, or

-C<sub>1</sub>-C<sub>6</sub> alkyl X-C<sub>1</sub>-C<sub>6</sub> alkyl aryl;

$$\begin{array}{c}
O \\
II \\
--CC_1-C_6 \text{ alkyl}
\end{array}$$

$$COC_1$$
- $C_6$  alkyl

O O II

$$-C-CH-NHCC_1-C_6$$
 alkyl

 $(CH_2)_n$ 

aryl or substituted aryl

$$\stackrel{O}{--}$$
CO(CH<sub>2</sub>)<sub>n</sub> aryl , or

 $R^6$  is hydrogen,  $C_1$ - $C_6$  alkyl, — $(CH_2)_n$  aryl, — $(CH_2)_nCO_2R^a$ , or hydroxyl substituted  $C_1$ - $C_6$  alkyl;

each n is independently 0 to 3,

provided that when  $R^{5a}$  is

$${\displaystyle \stackrel{O}{\longrightarrow}}_{CO(CH_2)_n}^{CO}$$
 aryl

then n is 0, 2, or 3, and

provided that when R<sup>5a</sup> is

$$\begin{array}{c} O \\ \parallel \\ - C(CH_2)_n \text{ aryl} \end{array}$$

then n is 0, 1, or 3,

and the pharmaceutically acceptable salts thereof.

## 53. (Currently Added) A compound of the Formula I

wherein R1 is

I

Application No. 09/284,424, filed 9 April 1999 Amendment and Response of 23 October 2003 Responsive to Office Action of 23 April 2003

Examiner: Leigh C. Maier

Group Art Unit: 1623

each  $R^a$  is independently hydrogen,  $C_1$ - $C_6$  alkyl, or -( $CH_2$ )<sub>n</sub> aryl;

$$R^{2} \text{ is } --(CRR)_{n}\text{-aryl},$$

$$--(CRR)_{n}\text{-X-aryl},$$

$$--(CRR)_{n}\text{-X-(substituted-aryl)},$$

$$--(CRR)_{n}\text{-aryl-aryl},$$

$$--(CRR)_{n}\text{-aryl-(CH}_{2})_{n}\text{-aryl},$$

$$--(CRR)_{n}\text{-CH}(aryl)_{2},$$

$$--(CRR)_{n}\text{-cycloalkyl},$$

$$--(CRR)_{n}\text{-X-cycloalkyl},$$

$$--(CRR)_{n}\text{-X-cycloalkyl},$$

$$--(CRR)_{n}\text{-CH}(CH_{2})_{n}\text{-aryl},$$

$$--(CRR)_{n}\text{-cycloalkyl},$$

Application No. 09/284,424, filed 9 April 1999 Amendment and Response of 23 October 2003 Responsive to Office Action of 23 April 2003

Examiner: Leigh C. Maier

Group Art Unit: 1623

each R is independently hydrogen, C<sub>1</sub>-C<sub>6</sub> alkyl, halogen or hydroxy;

X is O or S;

$$R^3 \text{ is } C_1\text{-}C_6 \text{ alkyl},$$
 
$$\text{aryl},$$
 
$$-(\text{CHR})_n\text{-aryl},$$
 
$$-(\text{CHR})_n\text{-substituted aryl},$$
 
$$O \\ || \\ -(\text{CRR})_n - C - OR^a,$$
 
$$-(\text{CRR})_n O(\text{CH}_2)_n\text{-aryl},$$
 
$$\text{cycloalkyl},$$
 
$$\text{substituted cycloalkyl},$$

$$-(CRR)_n - C - NR^aR^a$$

$$-(CRR)_n$$
 $-S$ 
 $-(CH_2)_n$  aryl
 $O$ 

$$-(CRR)_n - \overset{O}{\underset{II}{\parallel}} - C_1 - C_6 \text{ alkyl}$$

$$\begin{array}{c} O \\ II \\ \hline -(CRR)_n S(CH_2)_n COR^a \end{array}$$

$$\begin{array}{ccc} O & O \\ II & II \\ --(CRR)_nS(CH_2)_nCOR^a \\ II & O \end{array}$$

$$-(CRR)_nS(CH_2)_n$$
-aryl

$$\begin{array}{c} O \\ II \\ -(CRR)_n S(CH_2)_n - aryl \\ O \end{array}$$

$$O$$
 $\parallel$ 
 $-(CRR)_nSCC_1-C_6$  alkyl

$$O$$
 $\parallel$ 
 $CRR)_nS(CH_2)_n$  aryl

$$O$$
 $\parallel$ 
 $-(CRR)_nS(CH_2)_nCO_2R^a$ 

$$O_{II}$$
 $-(CH_2)_nNHCC_1-C_6$  alkyl

$$-(CH_2)_n^0CNR^bR^b$$

each R' is independently  $C_1$ - $C_6$  alkyl,

C<sub>1</sub>-C<sub>6</sub> alkylaryl,

aryl, or

hydrogen;

each J is independently

- $-CO_2R^b$ ,
- -CONRbRb,
- — $SO_2NR^bR^b$ , or
- $--SO_2R^b$ ;

each Rb is independently hydrogen, C1-C6 alkyl, aryl, substituted aryl, arylalkyl, or substituted arylalkyl;

R<sup>4</sup> is hydrogen,

C<sub>1</sub>-C<sub>6</sub> alkyl,

$$H_3CO-C-$$

-phenyl, or

$$C_1$$
- $C_6$  alkyl $-C$ -,

$$R^5$$
 is  $C_1$ - $C_6$  alkyl- $CO$ —,

$$--(CH2)naryl,$$

$$C_1$$
- $C_6$  alkylO $-C$ 

$$C_1$$
- $C_6$ -alkyl- $X$ - $(CH_2)_nCO$ ,

$$C_1$$
- $C_6$  alkyl- $X$ - $(CH_2)_nO$ - $C$ -

$$\begin{array}{c} O \\ -II \\ -C(CRR)_n aryl \end{array},$$

$${\rm \stackrel{O}{-}CNR^aR^a}_{,}$$

$$\begin{array}{ccc}
O & O \\
\parallel & \parallel \\
-C(CH_2)_nCNR^aR^a
\end{array}$$

$$\begin{array}{c} O \\ II \\ --CO(CH_2)_n \text{ aryl} \end{array},$$

$$\begin{array}{c} O \\ II \\ --CO(CH_2)_n \text{ substituted aryl} \end{array},$$

$$-\overset{O}{\underset{R^{6}}{\parallel}}-\overset{R^{a}}{\underset{R^{5a}}{\longleftarrow}}$$

$$--(CH_2)_nX(CH_2)_n$$
-aryl, or

—
$$C_1$$
- $C_6$  alkyl X- $C_1$ - $C_6$  alkyl aryl;

$$\begin{matrix} R^{5a} \text{ is} \\ & \overset{O}{--} CC_{1}\text{-}C_{6} \text{ alkyl} \,, \end{matrix}$$

$$-\frac{O}{II}$$
 $-COC_1-C_6$  alkyl

O O 
$$\parallel$$
 $\parallel$ 
 $-C-CH-NHCC_1-C_6$  alkyl  $(CH_2)_n$ 
 $\parallel$ 
aryl or substituted aryl

$$\begin{array}{c} O \\ II \\ -CO(CH_2)_n \ aryl \ , \ or \end{array}$$

 $R^6 \ \text{is hydrogen}, C_1\text{-}C_6 \ \text{alkyl}, --(\text{CH}_2)_n \ \text{aryl}, --(\text{CH}_2)_n \text{CO}_2 \\ R^a, \ \text{or} \\ \text{hydroxyl substituted} \ C_1\text{-}C_6 \ \text{alkyl};$ 

each n is independently 0 to 3,

provided that when R5a is

$$O$$
 $H$ 
 $CO(CH_2)_n$  aryl

then n is 0, 2, or 3, and

provided that when R<sup>5a</sup> is

$$-\frac{O}{C(CH_2)_n}$$
 aryl

then n is 0, 1, or 3,

and the pharmaceutically acceptable salts thereof.

## 54. (Currently Amended) A compound of the Formula I

wherein R1 is

$$R^3-C$$

Ι

Examiner: Leigh C. Maier

Group Art Unit: 1623

Application No. 09/284,424, filed 9 April 1999 Amendment and Response of 23 October 2003 Responsive to Office Action of 23 April 2003

Examiner: Leigh C. Maier

Group Art Unit: 1623

each Ra is independently hydrogen, C1-C6 alkyl, or -(CH2)n aryl;

$$R^2 \text{ is } \text{--}(CRR)_n\text{-aryl}, \\ \text{--}(CRR)_n\text{-X-aryl}, \\ \text{--}(CRR)_n\text{-X-(substituted-aryl)}, \\ \text{--}(CRR)_n\text{-aryl-aryl}, \\ \text{--}(CRR)_n\text{-aryl-}(CH_2)_n\text{-aryl}, \\ \text{--}(CRR)_n\text{-CH}(aryl)_2, \\ \text{--}CRR)_n\text{-cycloalkyl}, \\ \text{--}(CRR)_n\text{-X-cycloalkyl}, \\ \text{--}(CRR)_n\text{-X-cycl$$

$$-(CRR)_n-CH$$

$$(CH_2)_n-aryl$$

$$(CH_2)_n-aryl$$

$$-(CRR)_n$$
 —  $CH_{2}$  — substituted aryle  $(CH_2)_n$  — aryle

$$-(CRR)_n$$

each R is independently hydrogen,  $C_1$ - $C_6$  alkyl, halogen or hydroxy;

X is O or S;

$$R^3$$
 is  $C_1$ - $C_6$  alkyl,

$$--(CHR)_n$$
-aryl,

$$-(CRR)_n - \overset{O}{C} - OR^a$$

$$-(CRR)_nO(CH_2)_n$$
-aryl,

cycloalkyl,

substituted cycloalkyl,

$$-(CRR)_n - C - NR^aR^a$$

$$-(CRR)_n - \begin{matrix} O \\ II \\ S - (CH_2)_n \text{ aryl} \\ O \end{matrix}$$

$$-(CRR)_n - \overset{O}{\underset{\parallel}{\text{S}}} - C_1 - C_6 \text{ alky}$$

$$\begin{array}{c} O \\ II \\ --(CRR)_nS(CH_2)_nCOR^a \end{array}$$

$$-(CRR)_nS(CH_2)_nCOR^a$$

$$-(CRR)_nS(CH_2)_n$$
-aryl

$$-(CRR)_{n}^{O}S(CH_{2})_{n}-aryl$$

$$O$$
 $\parallel$ 
 $CCRR)_nSCC_1-C_6$  alkyl

$$O$$
 $\parallel$ 
 $CRR)_nS(CH_2)_n$  aryl,

$$\begin{array}{c}
O \\
II \\
-(CRR)_n S(CH_2)_n CO_2 R^a
\end{array}$$

$$-(CH_2)_nCNR^bR^b$$

each R' is independently C<sub>1</sub>-C<sub>6</sub> alkyl,

 $C_1$ - $C_6$  alkylaryl,

aryl, or

hydrogen;

each J is independently

 $-CO_2R^b$ ,

- ---CONRbRb,
- -SO<sub>2</sub>NR<sup>b</sup>R<sup>b</sup>, or
- $-SO_2R^b$ ;

each R<sup>b</sup> is independently hydrogen, C<sub>1</sub>-C<sub>6</sub> alkyl, aryl, substituted aryl, arylalkyl, or substituted arylalkyl;

R<sup>4</sup> is hydrogen,

$$C_1$$
- $C_6$  alkyl,

-phenyl, or

$$C_1$$
- $C_6$  alkyl $-C$ 

 $R^5$  is  $C_1$ - $C_6$  alkyl-CO—,

$$-(CH_2)_n$$
aryl,

$$C_1$$
- $C_6$  alkylO $-C$ -

$$C_1$$
- $C_6$ -alkyl- $X$ - $(CH_2)_nCO$ ,

$$C_1$$
- $C_6$  alkyl- $X$ - $(CH_2)_nO$ - $C$ -,

$$\begin{array}{c} O \\ -SC_{1}\text{-}C_{6} \text{ alkyl} \\ O \\ -SC_{1}\text{-}C_{6} \text{ alkyl} \\ O \\ -C(CH_{2})_{n}CNR^{a}R^{a}, \\ O \\ -CO(CH_{2})_{n} \text{ aryl}, \\ O \\ -CO(CH_{2})_{n} \text{ substituted aryl}, \\ O \\ -C(CRR)_{n}NHCO(CH_{2})_{n}\text{--aryl}, \\ O \\ -CC_{1}\text{-}C_{6} \text{ alkyl} X\text{-}C_{1}\text{-}C_{6} \text{ alkyl aryl}; \\ R^{5a} \text{ is} \\ O \\ -CC_{1}\text{-}C_{6} \text{ alkyl}, \\ \end{array}$$

-COC $_1$ -C $_6$  alkyl $_{, or}$ 

$$\begin{array}{c|c} O & O \\ \parallel & \parallel \\ -C-CH-NHCC_1-C_6 \text{ alkyl} \\ (CH_2)_n \\ \parallel & \text{aryl or substituted aryl} \end{array},$$

 $R^6$  is hydrogen,  $C_1$ - $C_6$  alkyl, — $(CH_2)_n$  aryl, — $(CH_2)_nCO_2R^a$ , or hydroxyl substituted  $C_1$ - $C_6$  alkyl;

each n is independently 0 to 3, and the pharmaceutically acceptable salts thereof.

55. (Currently Amended) A pharmaceutically acceptable ester, amide, or <u>other</u> prodrug of a compound of formula I according to Claim 1, wherein said ester is a C<sub>5</sub>-C<sub>7</sub> cycloalkyl ester or an arylalkyl ester.

Examiner: Leigh C. Maier Group Art Unit: 1623

- 56. (**Previously Added**) The pharmaceutically acceptable ester of a compound of formula I according to Claim 55.
- 57. (**Previously Added**) The pharmaceutically acceptable amide of a compound of formula I according to Claim 55.
- 58. (**Previously Added**) The pharmaceutically acceptable prodrug of a compound of formula I according to Claim 55.
- 59. (**Previously Added**) The pharmaceutically acceptable amide of a compound of formula I according to Claim 57, wherein said amide is derived from ammonia, primary C<sub>1</sub>-C<sub>6</sub> alkyl amines, and secondary C<sub>1</sub>-C<sub>6</sub> dialkyl amines; wherein the alkyl groups are straight or branched chain.
- 60. (**Previously Added**) The pharmaceutically acceptable amide of a compound of formula I according to Claim 57, wherein said amide is derived from ammonia, primary C<sub>1</sub>-C<sub>3</sub> alkyl amines, and secondary C<sub>1</sub>-C<sub>2</sub> dialkyl amines; wherein the alkyl groups are straight or branched chain.
- 61. (Cancelled).